**Appendix 2:** Nonserious adverse events reported in randomized controlled trials and observational studies of medical cannabinoid preparations (part 1 of 4)

	Type of study; no. (%) of events	
Adverse event*	Randomized controlled trials $n = 4615$	Observational studies n = 3553
Blood or lymphatic system disorders	26 (0.6)	0
Anemia	24	0
Leukopenia	2	0
Cardiac disorders	22 (0.5)	107 (3.0)
Palpitations	16	0
Tachycardia	6	107
Eye disorders	106 (2.3)	6 (0.2)
Photopsia	1	0
Blurred vision	105	6
Gastrointestinal disorders	758 (16.4)	558 (15.7)
Abdominal pain	3	2
Constipation	23	14
Diarrhea	45	29
Dry mouth	239	405
Dysphagia	13	0
Glossodynia	1	0
Mouth plaque	0	6
Mouth ulceration	5	4
Nausea	117	29
Oral mucosal disorder	0	12
Oral pain	12	28
Other gastrointestinal tract disorder	285	0
Pharyngitis	0	4
Tooth discolouration	0	11
Vomiting	15	14
General disorders and administration-site conditions	651 (14.1)	42 (1.2)
Application-site irritation	21	0
Asthenia	198	5
Chills	1	0
Edema	0	6
Fatigue	109	19
Feeling abnormal	1	0
Feeling drunk	24	0
Feeling hot	1	0
Hot flush	2	0
Hyperhidrosis	10	0

continued

**Appendix 2:** Nonserious adverse events reported in randomized controlled trials and observational studies of medical cannabinoid preparations (part 2 of 4)

Adverse event*         Randomized controlled trials n = 4615         Observational studies n = 3553           Influenza         2         0           Instillation-site foreign-body sensation         0         3           Loss of control of legs         0         2           Pain         278         5           Pallor         0         1           Pyrexia         0         1           Tenderness         1         0           Infections and infestations         134 (2.9)         0           Infections and infestations         134 (2.9)         0           Infections and infestations         134 (2.9)         0           Infections         134 (2.9)         0           Infections         134 (2.9)         0           Infections and infestations         134 (2.9)         0           Infections         134 (2.9)         0           Pull         2         0		Type of study; no. (%) of events	
Instillation-site foreign-body sensation         0         3           Loss of control of legs         0         2           Pain         278         5           Pallor         0         1           Pyrexia         0         1           Tenderness         1         0           Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)	Adverse event*	controlled trials	studies
Loss of control of legs         0         2           Pain         278         5           Pallor         0         1           Pyrexia         0         1           Tenderness         1         0           Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)         13 (0.4)           γ-Glutamyltransferase increased         0         6           Weight decreased         1         7           Metabolism and nutrition disorders         37 (0.8)         0           Anorexia         5         0           Increased appetite         32         0           Musculoskelatal, connective tissue and bone disorders         31 (7.2)         0           Arthralgia         1         0           Muscle spasm         2	Influenza	2	0
Pain         278         5           Pallor         0         1           Pyrexia         0         1           Tenderness         1         0           Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)         13 (0.4)           γ-Glutamyltransferase increased         0         6           Weight decreased         1         7           Metabolism and nutrition disorders         37 (0.8)         0           Anorexia         5         0           Increased appetite         32         0           Musculoskelatal, connective tissue and bone disorders         31 (7.2)         0           Arthralgia         1         0           Muscule spasm         289         0           Muscule weakness         4 <td>Instillation-site foreign-body sensation</td> <td>0</td> <td>3</td>	Instillation-site foreign-body sensation	0	3
Pallor         0         1           Pyrexia         0         1           Tenderness         1         0           Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)         13 (0.4)           γ-Glutamyltransferase increased         0         6           Weight decreased         1         7           Metabolism and nutrition disorders         37 (0.8)         0           Anorexia         5         0           Increased appetite         32         0           Musculoskelatal, connective tissue and bone disorders         331 (7.2)         0           Muscle spasm         289         0           Muscle spasticity         5         0           Muscle weakness         4         0           Muscle weakness	Loss of control of legs	0	2
Pyrexia         0         1           Tenderness         1         0           Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)         13 (0.4)           γ-Glutamyltransferase increased         0         6           Weight decreased         1         7           Metabolism and nutrition disorders         37 (0.8)         0           Anorexia         5         0           Increased appetite         32         0           Musculoskelatal, connective tissue and bone disorders         331 (7.2)         0           Arthralgia         1         0           Muscule spasm         289         0           Muscule spasm         289         0           Muscule twitching         21         0           Muscule weakness<	Pain	278	5
Tenderness         1         0           Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)         13 (0.4)           PGlutamyltransferase increased         0         6           Weight decreased         1         7           Metabolism and nutrition disorders         37 (0.8)         0           Anorexia         5         0           Increased appetite         32         0           Musculoskelatal, connective tissue and bone disorders         331 (7.2)         0           Musculoskeles spasm         289         0           Muscule spasm         289         0           Muscule weakness         4         0           Muscule weakness         4         0           Muscule weakness         4         0 <th< td=""><td>Pallor</td><td>0</td><td>1</td></th<>	Pallor	0	1
Thirst         3         0           Infections and infestations         134 (2.9)         0           Infection         134         0           Injury, poisoning and procedural complications         37 (0.8)         7 (0.2)           Drug toxicity         2         0           Fall         34         0           Joint injury         1         0           Poisoning         0         7           Investigations         1 (< 0.1)	Pyrexia	0	1
Infections and infestations Infection Infection Infection Injury, poisoning and procedural complications  Drug toxicity Pall Joint injury Investigations In	Tenderness	1	0
Infection1340Injury, poisoning and procedural complications37 (0.8)7 (0.2)Drug toxicity20Fall340Joint injury10Poisoning07Investigations1 (< 0.1)	Thirst	3	0
Injury, poisoning and procedural complications37 (0.8)7 (0.2)Drug toxicity20Fall340Joint injury10Poisoning07Investigations1 (< 0.1)	Infections and infestations	134 (2.9)	0
complicationsDrug toxicity20Fall340Joint injury10Poisoning07Investigations1 (< 0.1)13 (0.4)γ-Glutamyltransferase increased06Weight decreased17Metabolism and nutrition disorders37 (0.8)0Anorexia50Increased appetite320Musculoskelatal, connective tissue and bone disorders331 (7.2)0Arthralgia10Muscle spasm2890Muscle spasticity50Muscle weakness40Muscle weakness40Muscle weakness40Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Infection	134	0
Fall340Joint injury10Poisoning07Investigations1 (< 0.1)		37 (0.8)	7 (0.2)
Joint injury10Poisoning07Investigations1 (< 0.1)	Drug toxicity	2	0
Poisoning07Investigations1 (< 0.1)	Fall	34	0
Investigations1 (< 0.1)13 (0.4)γ-Glutamyltransferase increased06Weight decreased17Metabolism and nutrition disorders37 (0.8)0Anorexia50Increased appetite320Musculoskelatal, connective tissue and bone disorders331 (7.2)0Arthralgia10Muscle spasm2890Muscle spasticity50Muscle weakness40Muscle weakness40Muscle weakness40Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Joint injury	1	0
γ-Glutamyltransferase increased06Weight decreased17Metabolism and nutrition disorders37 (0.8)0Anorexia50Increased appetite320Musculoskelatal, connective tissue and bone disorders331 (7.2)0Arthralgia10Muscle spasm2890Muscle spasticity50Muscle twitching210Muscle weakness40Muscle weakness40Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Poisoning	0	7
Weight decreased         1         7           Metabolism and nutrition disorders         37 (0.8)         0           Anorexia         5         0           Increased appetite         32         0           Musculoskelatal, connective tissue and bone disorders         331 (7.2)         0           Arthralgia         1         0           Muscle spasm         289         0           Muscle spasticity         5         0           Muscle twitching         21         0           Muscle weakness         4         0           Musculoskeletal pain         2         0           Myalgia         7         0           Sensation of heaviness         2         0           Nervous system disorders         1695 (36.7)         1412 (39.7)           Abnormal dreams         2         0           Balance disorder         13         12           Cholinergic syndrome         0         1           Coordination abnormal         73         185	Investigations	1 (< 0.1)	13 (0.4)
Metabolism and nutrition disorders       37 (0.8)       0         Anorexia       5       0         Increased appetite       32       0         Musculoskelatal, connective tissue and bone disorders       331 (7.2)       0         Arthralgia       1       0         Muscle spasm       289       0         Muscle spasticity       5       0         Muscle twitching       21       0         Muscle weakness       4       0         Musculoskeletal pain       2       0         Myalgia       7       0         Sensation of heaviness       2       0         Nervous system disorders       1695 (36.7)       1412 (39.7)         Abnormal dreams       2       0         Balance disorder       13       12         Cholinergic syndrome       0       1         Coordination abnormal       73       185	$\gamma$ -Glutamyltransferase increased	0	6
Anorexia 5 0 Increased appetite 32 0 Musculoskelatal, connective tissue and bone disorders  Arthralgia 1 0 Muscle spasm 289 0 Muscle spasticity 5 0 Muscle twitching 21 0 Muscle weakness 4 0 Musculoskeletal pain 2 0 Myalgia 7 0 Sensation of heaviness 2 0 Nervous system disorders 1695 (36.7) 1412 (39.7) Abnormal dreams 2 0 Balance disorder 13 12 Cholinergic syndrome 0 1 Coordination abnormal	Weight decreased	1	7
Increased appetite320Musculoskelatal, connective tissue and bone disorders331 (7.2)0Arthralgia10Muscle spasm2890Muscle spasticity50Muscle twitching210Muscle weakness40Musculoskeletal pain20Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Metabolism and nutrition disorders	37 (0.8)	0
Musculoskelatal, connective tissue and bone disorders331 (7.2)0Arthralgia10Muscle spasm2890Muscle spasticity50Muscle twitching210Muscle weakness40Musculoskeletal pain20Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Anorexia	5	0
bone disorders  Arthralgia 1 0  Muscle spasm 289 0  Muscle spasticity 5 0  Muscle twitching 21 0  Muscle weakness 4 0  Musculoskeletal pain 2 0  Myalgia 7 0  Sensation of heaviness 2 0  Nervous system disorders 1695 (36.7) 1412 (39.7)  Abnormal dreams 2 0  Balance disorder 13 12  Cholinergic syndrome 0 1  Coordination abnormal	Increased appetite	32	0
Muscle spasm         289         0           Muscle spasticity         5         0           Muscle twitching         21         0           Muscle weakness         4         0           Musculoskeletal pain         2         0           Myalgia         7         0           Sensation of heaviness         2         0           Nervous system disorders         1695 (36.7)         1412 (39.7)           Abnormal dreams         2         0           Balance disorder         13         12           Cholinergic syndrome         0         1           Coordination abnormal         73         185		331 (7.2)	0
Muscle spasticity         5         0           Muscle twitching         21         0           Muscle weakness         4         0           Musculoskeletal pain         2         0           Myalgia         7         0           Sensation of heaviness         2         0           Nervous system disorders         1695 (36.7)         1412 (39.7)           Abnormal dreams         2         0           Balance disorder         13         12           Cholinergic syndrome         0         1           Coordination abnormal         73         185	Arthralgia	1	0
Muscle twitching210Muscle weakness40Musculoskeletal pain20Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Muscle spasm	289	0
Muscle weakness40Musculoskeletal pain20Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Muscle spasticity	5	0
Musculoskeletal pain20Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Muscle twitching	21	0
Myalgia70Sensation of heaviness20Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Muscle weakness	4	0
Sensation of heaviness 2 0 Nervous system disorders 1695 (36.7) 1412 (39.7) Abnormal dreams 2 0 Balance disorder 13 12 Cholinergic syndrome 0 1 Coordination abnormal 73 185	Musculoskeletal pain	2	0
Nervous system disorders1695 (36.7)1412 (39.7)Abnormal dreams20Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Myalgia	7	0
Abnormal dreams 2 0  Balance disorder 13 12  Cholinergic syndrome 0 1  Coordination abnormal 73 185	Sensation of heaviness	2	0
Balance disorder1312Cholinergic syndrome01Coordination abnormal73185	Nervous system disorders	1695 (36.7)	1412 (39.7)
Cholinergic syndrome01Coordination abnormal73185	Abnormal dreams	2	0
Coordination abnormal 73 185	Balance disorder	13	12
	Cholinergic syndrome	0	1
Dysarthria 0 1	Coordination abnormal	73	185
·	Dysarthria	0	1

continued

**Appendix 2:** Nonserious adverse events reported in randomized controlled trials and observational studies of medical cannabinoid preparations (part 3 of 4)

	Type of study; no. (%) of events	
Adverse event*	Randomized controlled trials n = 4615	Observational studies n = 3553
Dizziness	714	393
Dreamy state	16	0
Dysgeusia	22	11
Headache	79	21
Hypoesthesia	28	0
Hypotonia	0	4
Lethargy	0	6
Memory impairment	29	5
Migraine	1	0
Multiple sclerosis	31	5
Nervous system disorder (unspecified)	2	0
Neurologic visual problems not classified elsewhere	0	224
Paraesthesia	63	0
Paralysis	0	2
Sedation	100	517
Sensory disturbance	0	1
Somnolence	377	23
Spasticity	0	1
Syncope	29	0
Tinnitus	29	0
Tremor	71	0
Vertigo	16	0
Psychiatric disorders	512 (11.1)	1265 (35.6)
Abnormal dreams	0	149
Affect liability	3	0
Aggression	4	0
Anxiety	4	214
Confusional state	14	308
Delusional perception	18	0
Depression	93	193
Disorientation	28	0
Dissociation	34	0
Disturbance in attention	28	12
Euphoric mood	127	1
Feeling of despair	7	0
Hallucinations	15	0
Inappropriate affect	1	0

continued

**Appendix 2:** Nonserious adverse events reported in randomized controlled trials and observational studies of medical cannabinoid preparations (part 4 of 4)

	Type of study; no. (%) of events	
Adverse event*	Randomized controlled trials n = 4615	Observational studies n = 3553
Indifference	4	0
Irritability	5	0
Mental disorder	51	0
Mood altered	24	290
Nervousness	4	0
Panic attack	1	95
Paranoia	1	2
Psychomotor hyperactivity	1	0
Sleep disorder	0	1
Speech disorder	45	0
Renal and urinary disorders	236 (5.1)	0
Bladder disorder	222	0
Urinary tract infection	14	0
Respiratory, thoracic and mediastinal disorders	36 (0.8)	2 (0.1)
Cough	2	0
Dysphonia	1	0
Dyspnea	22	0
Нурохіа	0	1
Nasopharyngitis	4	0
Pharyngitis	4	0
Pulmonary embolism	0	1
Throat irritation	2	0
Upper respiratory tract infection	1	0
Skin or subcutaneous tissue disorders	30 (0.7)	0
Decubitus ulcer	4	0
Pruritus	11	0
Skin problem	15	0
Vascular disorders	3 (0.1)	141 (4.0)
Hypertension	2	0
Hypotension	1	141

<sup>\*</sup>Grouped by system order classes of the Medical Dictionary for Regulatory Activities.1

## Reference

 Medical dictionary for regulatory activities. Version 10.0. Los Angeles: Northrop Grumman Corporation; 2008. Available (by subscription): www.meddramsso.com/ (accessed 2008 Mar 25).